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**CIRQUE DU SOLEIL**

## BODY AND SOUL

*Combining Current Drugs  
 With a Vaccine Could Make a  
 Cure More Feasible*

# AIDS: The Next Step

BY MARK SCHOOFS

**A**lmost three years ago, top AIDS researcher David Ho was beginning the trial that would make eradication of HIV the goal of AIDS therapy. The idea was simple: Powerful drug combinations, including the new protease inhibitors, were able to stop the virus from replicating. Ho hoped the body would do the rest of the work, by clearing out all the cells infected with HIV.

"It's like a chess game," Ho said at the time. "If we are lucky enough to win, then great. But if we don't, understanding the moves the virus would make is still pretty useful."

Well, now we've seen HIV's next move. The vast majority of virus is indeed cleared by the body, but a tiny amount hides in certain immune system cells, where it lurks, dormant but able to reignite infection. Before this discovery, Ho estimated that HIV might be cleared in two years. Now, because HIV's accomplice cells persist in the body for a long time, he thinks it could take up to 20 years.

Unfortunately, it's not realistic to expect most patients to stay for that long on the powerful drugs—which are now being found to have significant side effects, and which must be taken on a strict schedule to prevent resistance. Bottom line: Suppressing the virus with current drugs isn't enough.

How, then, can doctors cure AIDS? They could try to flush out the Trojan-horse cells that harbor the virus. Several teams are trying this strategy, but the drugs they're using inflame the immune system, causing flu-like symptoms. Patients would likely have to endure several bouts of this treatment, yet at the end of it all, HIV might still be hiding in sanctuary cells the drugs don't reach.

But if doctors could strengthen the immune system so it can control small amounts of HIV, then every last virus wouldn't have to be eliminated. And that might make a cure a lot more feasible.

**BRUCE WALKER, A RESEARCHER** at Massachusetts General Hospital, tells a tale of two patients. One died just four years after he first got infected, the other shows no signs of disease after 18 years. What's the difference?

T-cells. These are the command-and-control arm of the immune system, marshaling attacks against invading germs. But each of the body's billions of T-cells recognizes only one germ—the flu virus, for example, or the tuberculosis bacterium. People with HIV whose immune systems never deteriorate retain T-cells that recognize the virus. But the vast majority of AIDS patients quickly lose their HIV-specific T-cells. As a result, the body cannot keep the virus under control, and the patient sickens and dies.

Recently, Walker found that if he treated people very soon after they were infected, suppressing their virus completely, these patients were able to preserve their HIV-specific T-cell response. Indeed, their immune systems appear

identical to those of long-term non-progressors.

But are they really the same? The acid test will be to take these quickly treated patients off therapy and see if they can control the virus. But even if they could keep HIV in check, the advance would not be very practical. Most people don't rush into care right after being infected—and that's especially true as the disease increasingly afflicts poor people who don't have access to good medical care. So the real question is whether people infected for a long time, whose HIV-specific T-cells have been wiped out, can get them back.

One approach is to take immune system cells out of the body, alter them in test tubes so that they recognize HIV, and then put them back. But Walker and Ho are trying to alter immune cells without removing them from the body. Their instrument? Vaccines, which train the immune system to recognize invaders.

Using an AIDS vaccine for therapy has been tried before, most notably by Jonas Salk.

**A RESEARCHER** tells a tale of two patients. One died four years after he got infected, the other shows no signs of disease after 18 years. What's the difference? T-cells.

But until recently, drugs couldn't suppress the AIDS virus, so the vaccines had to work in the midst of a raging HIV infection. Not surprisingly, they failed.

But now, with powerful drugs controlling the virus, Walker, Ho, and other researchers are about to start human trials using HIV vaccines to boost the immune system. Scientists are encouraged by signs that, on therapy, the immune system makes a slow comeback, even if it has been ravaged by the disease for years. But except in patients treated very early, it almost never returns to full strength. So can the immune system really be trained to cope with a virus as vicious as HIV?

Time and again in AIDS, promising ideas have been shattered by reality. The result is that the C-word—*cure*—has become a lightning rod. Utter it and you're bound to stir up a storm, as Ho has by championing the possibility of eradication.

What's really at stake here is raising false hopes—and, indeed, the vaccine approach may fail. But so what? The only alternative to pursuing a cure is to give up on a cure. And that's not an option. **V**